

Notice of Allowability

Application No.

09/889,273

Examiner

Fozia M Hamud

Applicant(s)

COX ET AL.

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/20/03.
2. ☒ The allowed claim(s) is/are 32-85 (renumbered 1-54, respectively).
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☒ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
 - * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No. _____.
 - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
 - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892) | 5 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6 <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____ |
| 3 <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____ | 7 <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8 <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

Examiner's Amendment:

1. An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R § 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the Issue Fee.

Authorization for this Examiner's Amendment was given in a telephone interview with Attorney Angela Dallas Sebor on 14 January 2004.

2. The application has been amended as follows:

IN THE CLAIMS:

- 2a. In claims 32, 35, 38, 40, line 3, after "host cell" delete "capable of".
- 2b. In claim 52, line 3, after "glutathionine," delete "or a derivative thereof,".
- 2c. In claim 35, line 7, after "glutathionine," delete "or a derivative thereof,".
- 2d. In claim 40, line 8, after "glutathionine," delete "or a derivative thereof,".
- 2e. In claim 35, line 6, after "cystine," insert --or a derivative thereof---
- 2f. In claim 40, line 7, after "cystine," insert --or a derivative thereof---
- 2g. In claim 52, line 2, after "cystine," insert --or a derivative thereof---
- 2h. In claim 62, line 2, after "bioassay," insert -- as measured by proliferation of a cell line that proliferates in response to growth hormone---
- 2i. In claim 69, line 2, after "bioassay," insert -- as measured by proliferation of a cell line that proliferates in response to erythropoietin---
- 2j. In claim 76, line 2, after "bioassay," insert -- as measured by inhibition of a cell line whose growth is inhibited in response to alpha interferon---

REASONS FOR ALLOWANCE:

3. The two primary references (Braxton and Cox) teach the production of proteins that have a free cysteine residue present in either the naturally occurring protein or introduced by site specific mutations, and a method of attaching PEG to said proteins.

However, neither Braxton nor Cox disclose a method of producing a soluble protein having a free cysteine by exposing a host cell expressing said protein to a cysteine blocking agent, wherein the cysteine blocking agent forms a mixed disulfide with at the least one cysteine residue and isolating the soluble protein from the host cell.

The secondary reference (Seely et al) disclose a method of isolating a recombinant protein, by first solublizing said protein by exposing it with a denaturing solution and then exposing the denatured protein to an oxidizing agent, such as cystine, to yield high bioactive monomeric proteins.

Although Seely et al reference suggest the addition of an oxidizing agent (cysteine blocking agent), to produce a bioactive protein, the cysteine blocking agent is introduced after the insoluble protein is isolated. However, the instantly claimed method introduces the cysteine blocking agent before the protein is isolated. This is significant, because the Applicant's method does not require reducing or denaturing steps to refold the protein. The instantly claimed invention produces a soluble protein having a free cysteine, which can be modified without a refolding step. Therefore, instant method saves time and cost.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-


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8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
20 December 2004


GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600